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JCM

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/435,403 11/05/99 LOLLAR

J 88-98

EXAMINER

023713 HM12/0312
GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER CO 80303

ART UNIT 2007 H PAPER NUMBER

1653 DATE MAILED:

5

03/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	FILE	Application No. 09/435,403	Applicant(s)
	Examiner Holly Schnizer	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) Responsive to communication(s) filed on 28 March 2000.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) All b) Some * c) None of the CERTIFIED copies of the priority documents have been:
1. received.
2. received in Application No. (Series Code / Serial Number) _____ .
3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 14) Notice of References Cited (PTO-892) 17) Interview Summary (PTO-413) Paper No(s). _____
- 15) Notice of Draftsperson's Patent Drawing Review (PTO-948) 18) Notice of Informal Patent Application (PTO-152)
- 16) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4. 19) Other: _____

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DETAILED ACTION

Status of the Claims

1. Claim 1 is pending.

Specification

2. The specification is objected to for the appearance of numbers such as <{33}> (p. 1, line 3), <{398}> (p. 1, line 5), <{11}> (p. 1, line 6). Such numbers appear throughout the specification and their meaning is unclear. Correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gething et al. (U.S. Patent No. 5,041,376; issued 1991) in view of Lollar (U.S. Patent No. 5,859,204; filing date 1996; submitted in IDS filed 3-28-00 as Paper No. 4).

5. Gething et al. teach a method of preparing proteins having modified glycosylation by (1) mutating the protein to encode an N-linked glycosylation site (-N-X-S/T) (see Col. 6, lines 41-48 and Col. 6, lines 58-68) and (2) expressing the mutant protein in a host cell capable of post-translational glycosylation whereby the protein with the modified

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glycosylation is prepared (see Col. 10, Ex. 6 and Col. 12-13, Ex. 9; Col. 9). (The entire method is also described at Col. 3, line 61 through Col. 4, line 19 and in the examples of Col. 9, beginning at line 39, through Col. 11). Gething et al. suggest that almost any protein could be used in the disclosed method (see Col. 7, lines 29-68 for examples of a variety of proteins that could be used in the method). Gething states that the purpose of adding the N-linked glycosylation site is to shield epitopes of naturally occurring proteins (Col. 3, lines 43-49) and that mutant proteins produced in the disclosed method are less likely to induce an immune response than other proteins that have been altered by genetic engineering; "a feature of importance if a protein engineered in this manner is to be administered as a drug" (Col. 15, lines 61-66).

6. Gething et al. do not disclose that factor VIII specifically could be used in the method.

7. Lollar teaches site-specific replacement of specifically defined amino acids in human factor VIII can result in reduction of reactivity to an inhibitory antibody (see abstract). Lollar states and at the time of the present invention it was commonly known that there is a significant interest in the development of a factor VIII that is less apt to cause production of inhibitory antibodies and a factor VIII molecule that evades immune detection in patients who have already acquired antibodies to human factor VIII (Col. 2, lines 36-46).

8. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to add N-linked glycosylation sites by site directed mutagenesis as

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taught in Gething et al. to the factor VIII molecule. The skilled artisan would have recognized, as illustrated in Lollar, a need for factor VIII molecules that evade immune detection and would have been motivated to look to Gething et al. for guidance of how to make proteins which are less likely to induce immune responses. Thus, Claim 1 is unpatentable over the prior art.

References cited but not relied upon:

9. Garrity et al. (U.S. Patent No. 5,585,250) is an additional reference which teaches that insertion of N-linked glycosylation sites into proteins by site-directed mutagenesis in order to reduce immune recognition of the protein is very well known in the art. Garrity et al. refer to the Gething et al. patent and state, "[t]he contemplated use of the N-linked modifications of the proteins is to increase the circulation time of the antigens by decreasing their immunogenicity" (Col. 2, lines 10-15). This statement illustrates that, at the time of the present invention, the skilled artisan would have looked to and recognized Gething et al. as a method of decreasing the immunogenicity of proteins by adding N-linked glycosylation sites.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached Monday-Friday from 7:30 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 306-4119. The fax phone number for Official Papers to this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Holly Schnizer, Ph.D.
March 8, 2001

Karen Cochrane Carlson Ph.D.

KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER

SERIAL NUMBER 09/435,403	FILING DATE 11/05/99	CLASS 435	GROUP ART UNIT 1646 1453	ATTORNEY DOCKET NO. 88-98
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APPLICANT JOHN S. LOLLAR, DECATUR, GA.

CONTINUING DOMESTIC DATA***
VERIFIED PROVISIONAL APPLICATION NO. 60/107,402 11/06/98

HS
371 (NAT'L STAGE) DATA***
VERIFIED

HS
None

FOREIGN APPLICATIONS***
VERIFIED

HS
None

IF REQUIRED, FOREIGN FILING LICENSE GRANTED 12/15/99

Foreign Priority claimed 35 USC 119 (e-d) conditions met	<input checked="" type="checkbox"/> yes <input type="checkbox"/> no	<input checked="" type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> Met after Allowance	STATE OR COUNTRY GA	Sheets Drawing 0	Total Claims 1	Independent Claims 1
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Verified and Acknowledged HS Examiner's Initials Initials

ADDRESS
GREENLEE WINNER AND SULLIVAN PC
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SUITE 201
BOULDER CO 80303

TITLE
GLYCOSYLATED, LOW ANTIGENICITY LOW IMMUNOGENICITY FACTOR VIII

FILING FEE RECEIVED \$890	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT NO. _____ for the following:	<input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____ <input type="checkbox"/> Credit
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